A Systematic Review of the Link between Childhood Obesity and Adult Cancers

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Abstract

Over the past three decades, Americans' rates of overweight and obese have steadily increased. It has been suggested that childhood obesity may increase the risk of cancer in adulthood. Much literature has focused on specific cancers or the mechanisms of obesity and its sequelae. Consequently, a systematic review is needed to more fully examine the relationship between childhood obesity and adult-related cancers. This review examined the evidence of the obesity and cancer relationship. A secondary aim was to determine the adult cancers most associated with childhood obesity. PubMed and Cinahl were searched during the fall of 2014. Criteria for inclusion were peer-reviewed articles published within the last ten years and included variables of interest of childhood obesity and adult-related cancer. Possible bias may be present because of intra-rater reliability. Other forms of bias could be from no unpublished articles or books being included and the review being science-oriented. Thirty out of a possible 658 articles were chosen for final review based on established parameters and applicability of information. Strong evidence was found supporting a link between childhood and adolescent obesity and specific types of adult cancers. A positive association was found with non-Hodgkin lymphoma and thyroid cancer in males and females; esophageal squamous cell carcinoma and colorectal adenoma in women; and renal cell carcinoma and colon cancer in males. A negative association was found with premenopausal breast cancer in women. Limited evidence of a positive association was found with colorectal and kidney cancers in males and females, and conflicting evidence was found for postmenopausal breast cancer in women. This review supports a link between childhood obesity and adult-related cancers and shows how these relationships may differ by gender. This review demonstrates the importance of efforts for early childhood obesity prevention to mitigate negative health outcomes later in life.

Chapter 1: Introduction

The world's population and especially Americans are becoming increasingly overweight and obese (Brawer, Brisbon, & Plumb, 2009). This overweight and obesity trend is also extending to and becoming more prevalent in younger ages (Gray, Lee, Sesso, & Batty, 2011). Childhood obesity is known to cause many adverse effects in childhood and later in life, including a perpetual state of obesity. It has been suggested that obesity in childhood may increase risks of certain cancers in adulthood (Brennan, Brownson, & Orleans, 2014).

Almost in parallel with obesity rates, cancer rates have also been increasing in the United States and worldwide (Must, Phillips, & Naumova, 2012). Four specific types of cancer have especially seen a significant increase in the last few decades; these types include non-Hodgkin lymphoma (Bertrand *et al*., 2013), renal cell carcinoma (Leiba *et al*., 2013), thyroid cancer (Kitahara, Gamborg, de González, Sørenson, & Baker, 2013), and esophageal adenocarcinoma (Etemadi *et al*., 2011).

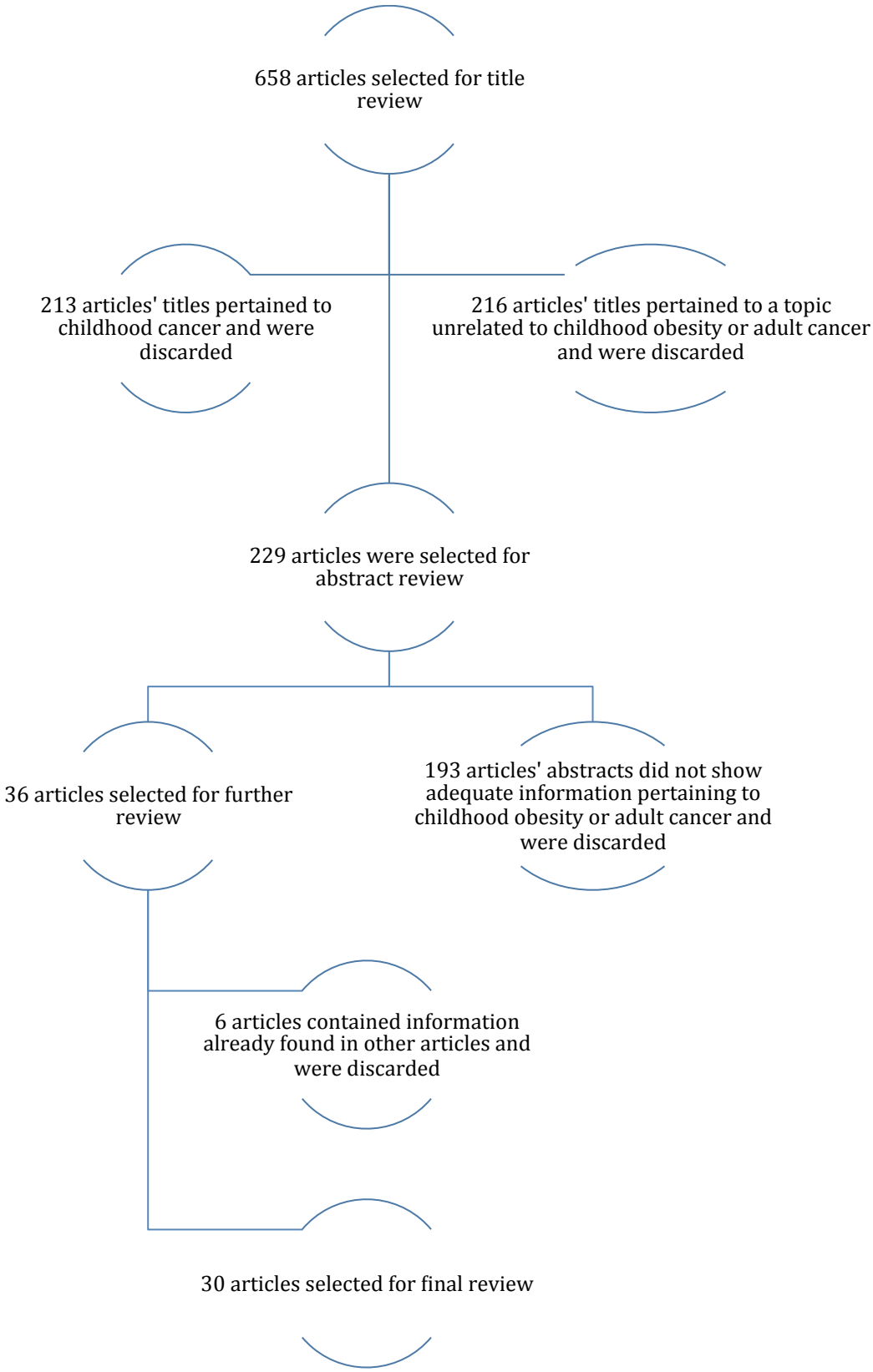
This trend of increasing rates in both obesity and cancer may suggest a co-morbid link between obesity and cancer, specifically lymphomas, renal cell carcinomas, thyroid cancer, and esophageal cancer. Although many peer-reviewed research articles focus on a specific type of cancer or the mechanisms of obesity and its sequelae, a systematic review is needed to more fully explore the connection between obesity, specifically that occurring during early life such as childhood or adolescence, and cancer. Such a systematic review would aid researchers, scientists, and health care practitioners in being able to synthesize the best evidence of the current literature on the possible obesity-cancer comorbidity. Nurses and other health care professionals would benefit from enhanced evidenced-based knowledge about the long-term effects of pediatric obesity and the necessity of prevention, early screening, and treatment.

In completing this systematic review, current knowledge on the effects of pediatric obesity on adult cancer was sought in the form of peer-reviewed published articles. The authors sought to determine the current state of the science and to identify gaps in the literature. The authors evaluated the strength of the evidence based on the review of studies using IOM recommendations. Finally, the review concluded with recommendations for research and practice.

Chapter II: Methods

Three databases were searched for peer-reviewed articles pertaining to childhood obesity and adult cancer during the fall of 2014. The databases included PubMed, Cinahl, and Cochrane Library. The search limitations were set to include only peer-reviewed articles published within the last ten years. The Cochrane Library database did not provide any results when the search terms pediatric obesity and adult cancer were used. Five articles were obtained from the Cochrane Library when the search terms childhood obesity and adult cancer were used; however, none of the studies were relevant to this review. The Cinahl database resulted in more relevant studies for inclusion. The search terms pediatric obesity and adult cancer identified 28 articles of which three were chosen for review. The search terms childhood obesity and adult cancer resulted in 61 articles with five of these being selected for review. The PubMed database included the most articles selected for review. Using the search terms pediatric obesity and adult cancer provided 181 potential articles of which eleven were chosen for review. The search terms childhood obesity and adult cancer resulted in 383 articles of which seventeen were selected for review. The initial review of abstracts included 36 articles of which 30 full text articles were included for the systematic review (see Figure 1).

Figure 1


658 articles selected for title review
213 articles' titles pertained to childhood cancer and were discarded
216 articles' titles pertained to a topic unrelated to childhood obesity or adult cancer and were discarded
229 articles were selected for abstract review
36 articles selected for further review
193 articles' abstracts did not show adequate information pertaining to childhood obesity or adult cancer and were discarded
6 articles contained information already found in other articles and were discarded
30 articles selected for final review

The thirty articles that were systematically reviewed were written in English. Eleven of the thirty articles provided pertinent background information regarding the mechanisms of obesity, measuring obesity in children, links between obesity and cancer, and health promotion and cancer prevention during childhood and adolescence. The remaining nineteen articles discussed studies and systematic reviews concerning obesity in childhood and its effects on adult health, a link between obesity in childhood and cancer in adulthood, the prevalence of obesity in childhood, and the effect of adverse childhood experiences on cancer in adulthood. Six of the thirty-six articles originally chosen for review were not included in this systematic review because they contained information already obtained from other articles.

A risk of bias is present for this review and should be considered in interpreting the findings. Only one person reviewed the articles and gathered the information, possibly influencing intra-rater reliability. No unpublished articles, dissertations, or evidence from books were included in the review. This review and the databases searched were science-oriented, which may have limited the reviewer's understanding of the scope of the problem.

Chapter III: Results

This review revealed a diverse number of variables in childhood and adolescence that may influence health outcomes in later adulthood. These variables and their related findings are further outlined in table 1. The key outcome variables for this review were height, weight, body fat, and associated BMI during childhood, adolescence, and early adulthood. Other variables, such as paternal or grandpaternal country of origin and height in adulthood, were not the focus of this study but were included as important contextual variables.

Table 1

Variable	Author(s) and Year of Publication	Findings
Adverse childhood experiences	Biro and Deardorff (2013), Korpimäki *et al*. (2010)	Disease in adulthood may be set into motion by early life factors that affect pubertal changes. However, having adverse childhood experiences was not conclusively associated with having cancer in adulthood.
Body fatness during early life	Baer *et al*. (2010), Bartle *et al*. (2013), Nimptsch *et al*. (2011)	Increased body fatness during childhood and adolescence was significantly associated with a decreased risk of breast cancer and an increased risk of colorectal adenoma in women. Obese children are more likely to gain more body fat than healthy-weight children.
Body size in adolescence	Sangaramoorthy *et al*. (2011)	Inverse associations were more likely between premenopausal breast cancer risk and relative weight than body build in Hispanic women. US-born women, who were more likely to have had larger childhood and adolescent body size, had strong inverse associations if they also currently had a BMI ≥25. No associations between postmenopausal breast cancer risk and childhood or adolescent body size were reported.
Body size throughout life	Möller *et al*. (2013), Bertrand *et al*. (2013)	Body size was not found to have any convincing association with prostate cancer although childhood overweight may increase the risk of fatal disease. The role of body size on non-Hodgkin lymphoma may be earlier than 18-21 years.
BMI in adulthood	Grey *et al*. (2011)	Increased BMI in early adulthood is associated with increased cancer rates, specifically of the lung, esophagus, skin, and urogenital areas.
BMI in childhood	Park *et al*. (2012), Bartle *et al*. (2013), Kitahara *et al*. (2013)	Being overweight in childhood was associated with cardiovascular outcomes and mortality, type 2 diabetes, hypertension, CHD, overall mortality, and thyroid cancer. There was also mixed evidence on an association with stroke outcomes and limited evidence of an association with colorectal and kidney cancers. Obese children are more likely to increase in BMI and unlikely to grow out of excess adiposity.
BMI in late adolescence	Leiba *et al*. (2013), Levi *et al*. (2011)	Being overweight during late adolescence is significantly associated with increased risk of renal cell carcinoma and colon cancer in adult males.
Health literacy skills of children, adolescents, and parents	Sanders *et al*. (2009)	Better outcomes with child health promotion and disease prevention are found in children with parents with higher literacy skills and adolescents with higher literacy skills. Large health systems and all government agencies need a health-literacy perspective.

Height in adulthood	Nimptsch *et al*. (2011)	Being taller as an adult was associated with an increased risk of colorectal adenoma.
Height in childhood	Kitahara *et al*. (2013), Must *et al*. (2012)	Increased childhood height was associated with greater risk of total thyroid cancer in adulthood and had some evidence of an association with follicular thyroid cancer risk. There was no evidence of a significant relationship with death from ischemic heart disease or ovarian cancer.
Obesity in adolescence	Inge *et al*. (2013), Reilly and Kelly (2011), Etemadi *et al*. (2011), Bertrand *et al*. (2013)	Adolescent obesity was positively associated with increased risk of esophageal squamous cell carcinoma in women and bariatric surgery earlier in adulthood, premature mortality and adult morbidity, and non-Hodgkin lymphoma in both men and women.
Outcomes of obesity in childhood	Reilly and Kelly (2011), Bertrand *et al*. (2013), Berenson (2012)	Childhood obesity was associated with increased risk of premature mortality, adult morbidity, heart diseases, diabetes, and non-Hodgkin lymphoma.
Paternal or grandpaternal country of origin	Leiba *et al*. (2013)	Being of European descent is strongly related to renal cell carcinoma in adult males.
Physical activity in childhood	Etemadi *et al*. (2011)	Sedentary work was a contributing risk factor for esophageal squamous cell carcinoma development in women.
Weight in childhood	Must *et al*. (2012)	Increased childhood weight significantly increased the risk of death from ischemic heart disease, breast cancer, and ovarian cancer.

Three articles focused on body fatness during childhood or adolescence and its relationship with cancer later in life. Baer, Tworoger, Hankinson, & Willett (2010) gathered data from two cohort studies, the Nurses' Health Study (NHS) and the Nurses' Health Study II (NHS II), in their prospective analysis regarding the risk of breast cancer in females. They found a strong, significant inverse association between greater body fatness in childhood and adolescence and breast cancer risk throughout life. Bartle, Hill, Webber, van Jaarsveld, & Wardle (2013) conducted a secondary analysis of data from a cohort study focusing on exercise and appetite in London schoolchildren. Their results indicate that it is highly unlikely that "obese pre-adolescent children 'grow out of' excess adiposity" (p. 421). Furthermore, Nimptsch *et al.* (2011) utilized

data from NHS II to determine a significant association between higher body fatness at age 5 and increased risk of colorectal adenoma in women.

Body Size, Body Mass Index, and Cancer

Three articles examined the role of body size in childhood and adolescence to cancer. Sangaramoorthy, Phipps, Horn-Ross, Koo, & John (2011) described a population-based case-control approach to the relationship between childhood and adolescent body size and risk of breast cancer in Hispanic women in the San Francisco Bay area. They found an inverse association between larger body size in childhood and adolescence and premenopausal breast cancer risk and no association between body size in childhood and adolescence and postmenopausal breast cancer risk. Möller *et al.* (2013) also employed a population-based case-control approach in a study of lifetime body size and prostate cancer risk among Swedish men. They reported no significant relationship between body size and prostate cancer although there was a possible link between larger childhood body size and the risk of fatal disease. Bertrand *et al.* (2013) conducted a secondary analysis of data from two cohort studies, NHS and the Health Professionals Follow-up Study (HPFS), to study the relationship between body size and risk of non-Hodgkin lymphoma (NHL). They found that "larger body size in childhood, adolescence, and young adulthood predicts an increased risk of NHL in both men and women" (p. 871).

Grey, Lee, Sesso, & Batty studied the relationship between body mass index (BMI) in early adulthood and cancer. Grey *et al*. (2011) relied on data from the Harvard Alumni Health Study, an ongoing prospective cohort study, and death certificates from state departments. The researchers were specifically interested in the link between BMI in early adulthood and later mortality from site-specific cancers. Their findings indicated an 8% increase in the risk of cancer-related death with every 1 SD increase in BMI in early adulthood. They also found that

increased BMI in early adulthood was associated with increased cancer rates, especially of the lung, esophagus, skin, and urogenital areas.

Three articles examined the effect of being overweight in childhood and cancer later in life. Must *et al*. (2012) investigated data from the Third Harvard Growth Study, a longitudinal cohort study, to explore a relationship with mortality risk from breast or ovarian cancer. The researchers found that women who had ever been overweight in childhood were twice as likely to die from breast cancer than those who had not been overweight in childhood. They also found no relationship between ovarian cancer and ever being overweight in childhood.

Park, Falconer, Viner, & Kinra (2012) systematically reviewed articles on the relationship between childhood BMI and adult disease risk. Their findings suggest limited evidence of an association between childhood overweight and colorectal and kidney cancers and mixed results were found between childhood overweight and breast cancer risk. Kitahara *et al.* (2013) utilized the Copenhagen School Health Records Register and the Danish Cancer Registry to examine childhood BMI and adult thyroid cancer. Their findings support a relationship between increased BMI during ages 7-13 and increased risk of thyroid cancer, especially papillary, and a nonsignificantly stronger association among men.

Childhood Obesity and Cancer. Two articles examined childhood obesity and the risk of cancer in adulthood. Reilly & Kelly (2011) conducted a systematic review on the associations between childhood obesity and various types of cancer. They found a significantly increased risk of pre- and postmenopausal breast cancer and other non-smoking-related cancers with childhood obesity. Berenson (2012) wrote about the findings of the Bogalusa Heart Study. This study reported that childhood obesity rates are trending upward and thus their resulting affects on health are also increasing.

Adolescent Overweight, Obesity, and Cancer. Two studies focused on the effects of being overweight in late adolescence and adult cancers. Leiba *et al.* (2013) employed a male-only population-based cohort study to examine the relationship between adolescent BMI and risk of renal cell carcinoma (RCC). They found a strong association between adolescent overweight and RCC. Levi *et al.* (2011) also used a male-only population-based cohort study to explore the link between adolescent BMI and risk of colorectal cancer. They discovered a significant, positive relationship between overweight BMI and colon cancer, but no relationship between BMI and rectal cancer. Three articles focused on the effects of obesity in adolescence and adult cancers. Inge *et al.* (2013) gathered data from the Longitudinal Assessment of Bariatric Surgery-2, an observational cohort study. They found that "the risk of numerous comorbid conditions was significantly elevated by adolescent obesity, independent of change in BMI since adolescence" (p. 1101). Reilly & Kelly (2011) reported no significant relationship between adolescent obesity and risk of breast cancer. Etemadi *et al.* (2011) examined data from a case-control study to determine the association of adolescent obesity with esophageal squamous cell carcinoma (ESCC). They concluded that there is a positive association between adolescent obesity and risk of ESCC in women.

Factors Associated with Obesity and Cancer

Three articles examined at the effects of factors associated with obesity and cancers. Biro & Deardorff (2013) described the effects of early life events on adult morbidities. They reported a decreased risk of developing breast cancer with delayed menarche, an association between earlier maturation and higher BMI, and an increased risk of developing breast cancer with exposure to radiation during childhood and adolescence. Korpimäki, Sumanen, Sillanmäki, & Mattila (2010) utilized the Health and Social Support Study, a prospective follow-up study of

psychosocial health, in their search for a link between adverse childhood experiences and adult cancer. They found "no conclusive evidence that childhood adversities affect risk of cancer in working age" (p. 440). Etemadi *et al.* (2011) examined the relationship between sedentary work in adolescence and ESCC and found a significant association between the two in women.

Twelve articles provided essential background information on obesity and cancer. Sanders, Shaw, Guez, Baur, & Rudd (2009) reported a positive relationship between higher health literacy skills of children, adolescents, and parents and child health outcomes. Tam & Ravussin (2012), de Pergola & Silvestris (2013), Hursting & Dunlap (2012), and Hursting & Hursting (2012) gave information on the different pathways in the body that are associated with obesity and cancer and recommended that more research be done to determine the strength of the relationship between cancer and specific components of these pathways. Brennan *et al.* (2014); Goran & Ventura (2011); Brawer *et al.* (2009); and Biro & Wien (2010) examined strategies to prevent obesity in childhood, including involvement of the whole family and community and changes in diet and environment. Cowie (2014) looked at the current tools and strategies, including BMI and national reference data, for measuring overweight and obesity in children and their effectiveness. Barness, Opitz, Gilbert-Barness (2007) and Crocker & Yanovski (2011) explored options to treat obesity in childhood, including a well-balanced diet with other treatments such as medications and surgery. These articles enhanced the reviewers' understanding of the link between obesity and cancer and offered some direction for how research should be continued and how prevention should be pursued.

Chapter IV: Discussion

This systematic review summarizes the available peer-reviewed literature published that examined relationships between obesity in childhood and/or adolescence and the subsequent risk

of cancer in adulthood. The evidence suggests a strong link between childhood obesity and many adult-related cancers. Some cancers were more strongly linked than others, such as non-Hodgkin's lymphoma and thyroid cancer (see Table 2). Other cancers were gender specific, such as esophageal squamous cell carcinoma in women and renal cell carcinoma in men.

Table 2

Variable	Positive association	Negative association	Limited association	No association
Childhood overweight	Breast	Mixed: breast	Kidney, colorectal	Ovarian
Childhood obesity	Non-smoking related, postmenopausal breast, premenopausal breast			
Either in childhood	Thyroid, colorectal adenoma in women		Prostate	
Adolescent overweight	Renal cell carcinoma, colon			Rectal
Adolescent obesity	Esophageal squamous cell carcinoma in women			Breast
Either in adolescence	Urogenital, skin, lung, esophagus, all cancers			
All of the above	Non-Hodgkin lymphoma	Premenopausal breast, breast		Prostate, postmenopausal breast

The review showed mixed results in linking breast cancer and early-life obesity. Some studies found a strong negative relationship (Baer *et al*., 2010) and others found a strong positive association (Must *et al*., 2012). This review concludes that the best evidence currently shows that there is a link between early-life obesity and breast cancer, especially the premenopausal type.

The review further revealed mixed results regarding the link between childhood and adolescent overweight and colorectal cancer. One study found a strong link between greater body fatness in childhood and colorectal adenoma in women (Nimptsch *et al*., 2011). Another study found a strong link between adolescent overweight and colon cancer in men (Levi *et al*., 2011)

while a similar study found no link between adolescent overweight and rectal cancer in men (Leiba *et al*., 2013). Thus, colorectal cancer has differing relationships with early-life weight depending on gender.

Some other cancers were positively associated with increased BMI in early life including the lung, skin, esophagus, and urogenital areas (Grey *et al*., 2011). A strong relationship was found between adolescent obesity and esophageal squamous cell cancer in particular in women (Etemadi *et al*., 2011). Although only a limited association was found between childhood overweight and kidney cancer (Park *et al*., 2012), a strong association was found between adolescent overweight and renal cell carcinoma in males (Leiba *et al*., 2013). Non-Hodgkin's lymphoma was associated with increased body weight during childhood and adolescence in both men and women (Bertrand *et al*., 2013). Thyroid cancer was also associated with increased BMI at young ages with a nonsignificantly stronger association with men (Kitahara *et al*., 2013).

Other studies on the processes of obesity support the link between obesity and cancer. Two articles explained the inflammatory processes of obesity and the way that these processes can lead to cancer (Hursting & Hursting, 2012). They determined that "obesity is an established risk and progression factor for many cancers" (Hursting & Dunlap, 2012, abstract). De Pergola & Silvestris (2013) found that endometrial, esophageal adenocarcinoma, colorectal, postmenopausal breast, prostate, and renal cancers were the most commonly found cancers in obese people. Malignant melanoma, thyroid cancer, leukemia, non-Hodgkin's lymphoma, and multiple myeloma were less commonly found in obese people. Our review also found a link between several of these cancers and increased weight in early life. Other research confirms that a high BMI in childhood predisposes to obesity in adulthood and all of the associated chronic conditions (Tam & Ravussin, 2012).

These findings have several implications for the medical field and especially nurses. Nurses must be careful not to let their bias cause them to treat obese patients any differently than other patients. They must also ensure that the findings of this review do not cause them to view cancer patients in a different light. Clinicians should be aware that an obesity epidemic will increase costs in medical care and further drain already limited resources. Thus, they should be involved in efforts to curb this epidemic and educate the public on the consequences of allowing the obesity epidemic to continue.

Chapter V: Conclusions

Based on this systematic review, several recommendations are suggested. First, primary prevention of overweight and obesity in childhood is key to stemming the growing number of adults with cancer. Primary prevention starts with parental education support and multi-level family focused initiatives. Goran & Ventura (2011) found that childhood weight status was linked to parental lifestyle factors including maternal pregnancy weight, eating habits, allowance of screen time, and attitude toward physical activity. Specific recommendations for the primary prevention of childhood obesity generally accepted in the literature include limiting sugar-sweetened beverages, meals at fast-food restaurants, screen time to two hours daily, televisions in bedrooms, and energy-dense foods; and encouraging sixty minutes of daily physical activity, eating meals as families, increased fruit and vegetable consumption, eating breakfast, and using organic foods (Biro & Wien, 2010). Most of these preventive recommendations are targeted at families and family initiatives.

To be more successful, primary prevention efforts must expand beyond behavioral interventions and target other determinants of health. For example, “children of parents with higher literacy skills and adolescents with higher literacy skills are more likely to have better

outcomes in child health promotion and disease prevention" (Sanders *et al.*, 2009, p. S312). Furthermore, researchers, clinicians, and healthcare providers must develop evidenced-based strategies that target broader determinants beyond the family and home environments. Brawer *et al.* (2009) determined that prevention should involve the whole community incorporating families, schools, and clinicians to combat obesity before it is obvious and hard to control. Health care providers and health professionals must begin to shift the social norms in local communities, often beginning with family awareness during routine screenings and care.

Because routine calculation of overweight and obesity status by pediatricians, health care providers, and school nurses are important to primary and secondary prevention (Goran & Ventura, 2011), the methods of determining childhood weight, body mass index, and associated health status must be consistent across all care settings. Cowie (2014) found that practitioners routinely use a variety of methods in assessing childhood overweight and obesity. Cowie concluded that BMI is the accepted tool for assessment of overweight and obesity in children but must be used with caution and that national reference data is better than international reference data and percentile curves for determining a child's weight status. Furthermore, practitioners should be trained to properly use anthropometric measurements and must use their knowledge and professional judgment when assessing weight status of children.

Once diagnosed, tertiary preventive efforts become essential. Behavioral and medical treatment options are available to mitigate obesity. In some communities, many of these options are not available or discussed with parents of obese children. This review has found that most health care providers begin with behavioral interventions rather than other medical alternatives. The behavioral interventions mirror that of primary prevention, but the key to treating obesity is behavioral changes (Crocker & Yanovski, 2011). Limited intake of a well-balanced diet leading

to gradual weight reduction and eventually weight maintenance is promoted (Barness *et al.*, 2007). Medical interventions include medications and surgical interventions. These are often reserved for use if behavioral interventions fail. Bariatric surgery has become an option if other treatment options fail or the obesity is extreme before help is solicited (Crocker & Yanovski, 2011).

Finally, nurses are on the front line of care and should take the lead in mitigating the childhood obesity epidemic. Because sustainable strategies for prevention of childhood obesity remain a challenge to health care providers, clinicians, and researchers (Brennan *et al.*, 2014), nurse researchers and nurse clinicians can be exploring new strategies and evidenced-based initiatives. As leaders, nurses can begin by advocating for broad policy changes to impact school and community environments. For example, policies targeting school lunch programs, physical education requirements, sugar-sweetened beverages, and active community initiatives are often led by nurse leaders in schools and communities. Nurses are also at the forefront of educating parents and children on healthy lifestyle choices and behavioral change. At all levels of prevention, nurses are essential leaders of care provision, advocacy, and change. These three things are the key to reducing the number of children and adolescents that are obese and the resulting number of adults with cancer.

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